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Oral cancer in young Jordanians: potential association with frequency of narghile smoking

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Objective. The aim of this study was to investigate the relationship between narghile (water-pipe) smoking and the age of patients when diagnosed with oral cancer.
Study Design. Patients with oral cancer registered in the Jordanian National Cancer Registry were asked about frequency of cigarette, narghile, and alcohol use. Relationship between age at diagnosis and risk factors was assessed using multiple regression analysis.
Results. In this sample, 66% of patients were cigarette smokers, and 36% and 17% were narghile smokers and alcohol drinkers, respectively. The multivariate regression analysis adjusted for sex, cigarette smoking, and alcohol drinking found that narghile smokers were significantly younger when diagnosed with oral cancer compared with nonsmokers.
Conclusions. Narghile smoking is an independent risk factor associated with the development of oral cancer at a younger age. Prospective studies of its effect on the earlier development of oral cancer are needed to establish a cause-effect relationship.
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Cancer is a major health problem worldwide, with more than 14 million new cancer cases and more than 8.2 million deaths reported annually throughout the world.[1] Oral cancer is ranked among the top 10 cancers worldwide. However, this ranking shows high variation between countries. For example, whereas oral cancer is the ninth most common cancer in the Eastern Mediterranean region, the ranking jumps to number 1 in men from countries of the Indian subcontinent.[2] This regional variation is believed to be related to lifestyle risk factors practiced by different communities.

Most oral cancers are histologically squamous cell carcinomas that are linked to unhealthy lifestyle habits (such as tobacco smoking, alcohol drinking, and forms of smokeless tobacco) and to high-risk types of human papillomavirus.[3] Tobacco's health hazards have been extensively studied, particularly in relation to cancer.

One of the forms of smoking tobacco is narghile, also called sheesha, hubble-bubble, water-pipe, hooka, and arghila. It consists of flavored tobacco that is burnt by a charcoal and inhaled through a water-filled glass container. There is a general misperception that this method of inhaling burnt tobacco is less harmful,[4,5] despite the high concentration and large volume of carbon monoxide generated.[6-9] Narghile's effect on the cardiovascular system is evident in causing endothelial cell dysfunction,[10] in decreasing heart rate variability, and in increasing blood pressure and heart rate.[11] Narghile smoking was found to increase nicotine concentration in the blood,[12] a finding that can explain its association with dependence.[13,14] Narghile not only is addictive but also is seen as a factor that leads to the habit of cigarette smoking.[15,16]

Narghile smoking has significant associations with diseases of the respiratory system (including lung cancer) and low birth weight, and it has possible associations with bladder, nasopharyngeal, and esophageal cancers and oral epithelial dysplasia.[17]

Narghile smoking is becoming a fashion among youth, but it is not a recent form of tobacco smoking. For centuries, narghile has been confined to Middle Eastern and Asian communities.[18] With migration to the west, migrants carried this traditional smoking method to their new habitat, which was transferred to their succeeding generations. This was evident in some studies that found that a relatively high percentage of American youth of Arab decent preferred this smoking method compared with their non-Arab American counterparts, who preferred cigarettes.[19] Other studies

Statement of Clinical Relevance

This study found an important association between narghile (water-pipe) smoking and oral squamous cell carcinoma at a younger age of diagnosis.

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found that narghile smoking is not restricted to specific communities but rather is a habit quickly spreading among the youth in many places in the world.[15,19-22] For example, in the United States, studies found that between 10% and more than 20% of high school students reported smoking narghile.[23,24] Another study performed among secondary school students in London found that nearly one-quarter of students have tried narghile smoking and that 7.6% were current narghile smokers.[25]

Despite worldwide awareness campaigns on smoking health hazards, the prevalence of narghile smoking is rising. A prospective longitudinal study in which Jordanian school teenagers were followed up for a period of 2 years found an increase in the prevalence of current narghile smoking from 13.3% to 18.9%.[26] Prevalence studies among Jordanian university students found rates between 30% and 40%,[27,28] which were similar to the rates among university students in other countries.[29,30]

This pervasion of narghile smoking among the younger generations, particularly girls and young women,[20] can be explained by the perception of narghile smoking as being associated with joyful gatherings and togetherness. Another encouraging factor for young people is the fact that this method is socially acceptable compared with cigarette smoking, which is often seen as stigmatizing.[4,18,31] As a result, narghile's prevalence was found to be fairly distributed among people from various socioeconomic classes compared with cigarette smoking, which was more prevalent among richer people.[27] Narghile smoking by parents and family members was found to be an encouraging factor for youngsters to start this habit.[20]

Jordan, an Arabian Middle Eastern country, has a population of 6.39 million.[32] Between 1996 and 2008, more than 21 000 Jordanians were diagnosed with cancer. Among those, 729 (3.3%) had cancers affecting the lip, mouth, and pharynx.[33] No data on the prevalence of tobacco and alcohol use among those patients with cancer are available. The rapid spread of narghile smoking among young people in different parts of the world[18-31] and the lack of data on the topic of narghile-associated diseases in younger persons serve as the impetus of this research. In this study, we investigated the relationship between the frequency of narghile smoking and the age of cancer development in a cohort of Jordanian patients previously diagnosed with squamous cell carcinoma.

MATERIALS AND METHODS

All cases of oral cancer registered with the Jordanian National Cancer Registry between the years 1996 and 2008 were identified and extracted. Sites included in this study were the lip (excluding the external lip), mouth, and oropharynx, identified by codes C00-C10 of the International Classification of Diseases for Oncology, Third Edition, excluding C08 (salivary glands). Inclusion criteria were biopsy-proven squamous cell carcinoma, Jordanian nationality, and valid patient contact details.

Personal information and tumor characteristics were collected from each case file. Participants were telephone-interviewed by 2 research assistants who were trained in cancer data collection and patient communication by the National Cancer Registry. Participants were asked if, before their cancer diagnosis, they smoked cigarettes, smoked narghile, drank alcohol, or had any combination of those habits. Those who answered positively were asked about the frequency of their consumption. Answers were entered into an online survey form, then extracted into Excel 2010 (Microsoft Corp, Redmond, WA, USA). Data were later categorized based on duration and frequency of use of tobacco and alcohol; regularity of use was defined as being a cigarette smoker of at least 10 cigarettes per day and an alcohol drinker at least once per month in the 3 years before cancer diagnosis. Frequency of narghile smoking was determined by asking patients to choose the best option that describes their narghile use during the 3 years before their cancer diagnosis: Daily, a few times per week, a few times per month, a few times in life, or never. Participants were then clustered into regular users (if daily use or a few times per week to a few times per month) or occasional users (a few times per year). Those who never used or used only a few times in their lives were considered nonsmokers. Deceased patients were excluded from this study.

Statistical analysis

IBM SPSS/PASW, version 20 (IBM Corp), was used for data processing and analysis. Descriptive statistics were computed for the total sample. Participant characteristics were described using frequency distribution for categorical variables and means and SDs for continuous variables. Independent t test was used to assess the association between age at diagnosis and sex according to frequency of narghile smoking (regular, occasional, or never). Analysis of variance was also used to evaluate the bivariate association between age at diagnosis and narghile smoking. Additional multiple regression analysis was used, in which the association between age at diagnosis (dependent variable) and narghile smoking (independent variable) was examined, after adjustment for alcohol drinking, cigarette smoking, and gender. In this analysis, age at diagnosis in regular and occasional narghile smokers was compared with the age in nonsmokers (reference group). Parameter estimates with 95% CIs were calculated and reported with P values.

Table I. Demographic data of participants

Variable	*Value, n (%) (N = 102)*
Gender	
Male	69 (68)
Female	33 (32)
Age (y) at diagnosis	
Mean (SD)	57.6 (17.5)
Level of education	
Primary and secondary education completed	45 (44)
University completed	39 (39)
Illiterate	17 (17)
Marital status	
Married	96 (94)
Single/widowed/divorced	6 (6)
Occupation before cancer diagnosis	
Office work	38 (37)
Unemployed/Retired	33 (32)
Vocational	23 (23)
Farming	34 (34)

Table II. Lifestyle risk factors (use of narghile, cigarettes, alcohol)

Variable	*n (%)*
Cigarette smoker	
Yes	67 (66)
No	35 (35)
Narghile smoker*	
Yes	37 (36)
No	65 (64)
Alcohol drinker	
Yes	17 (17)
No	85 (83)
Cigarette and alcohol	
Yes	12 (12)
No	89 (87)
Cigarette and narghile smoking	
Yes	22 (22)
No	79 (78)
Narghile and alcohol	
Yes	11 (11)
No	89 (89)
Cigarette, narghile, and alcohol	
Yes	2 (2)
No	98 (98)

Numbers in some categories may not add up to 102, owing to missing data.
*User (ever) in the 3 years before cancer diagnosis.

Ethical approval

This study was approved by the Research Ethics Committee of the Ministry of Health in Jordan (No. FM/927/52811) and the Research Ethics Committee at the University of Sharjah in the United Arab Emirates.

RESULTS

Between the years 1996 and 2008, 620 patients were diagnosed with cancer of the lips, mouth, or oropharynx. Of those, there were 318 who had complete records that contained biopsy-proven diagnosis of squamous cell carcinoma and who were Jordanian nationals; 128 had valid contact phone numbers. During this study, 26 patients were found to be deceased and were excluded. More than two-thirds of our patients were men (n = 66; 68%), with a mean age of 58 years (SD, 17.5 years). The majority were married and literate (Table I).

Table II shows the number of patients who considered themselves regular users of common lifestyle risk factors, namely tobacco and alcohol. The majority of patients were regular cigarette smokers (66%); fewer were regular alcohol drinkers (17%); and more than one-third were narghile smokers (36%).

Table III shows the association between age at diagnosis and narghile smoking by gender. Both male and female patients who smoked narghile were significantly younger when they were diagnosed with cancer. The frequency of narghile smoking was inversely associated with the age at cancer diagnosis.

The bivariate association between age at diagnosis and the independent variables considered in this study is displayed in Table IV, in which increase in frequency of narghile smoking was significantly associated with younger age at cancer diagnosis. This association persisted in the multivariate model, after adjustment for gender, cigarette smoking, and alcohol drinking (Table V). Of note, regular narghile smoking was associated with an average decrease in age of diagnosis of 16.44 years compared with nonsmokers (95% CI, −26.33 to −6.55). Similarly, occasional narghile smokers were diagnosed on average 11.79 years younger than nonsmokers (95% CI, −23.29 to −0.27).

DISCUSSION

Although oral squamous cell carcinoma is more common in middle-aged to elderly men, an increasing incidence is seen among younger people.[34] This is thought to be related to changes in lifestyle risk factors. The aim of this study was to assess the frequency of risk factors (tobacco smoking and alcohol drinking) among a cohort of patients with oral squamous cell carcinoma and to explore the association between those risk factors and the age at the time of oral cancer diagnosis.

In Jordan, oral cancer is not among the top 10 most common cancers,[1] and little is known about its risk factors in this country, where the societal acceptance of cigarette and narghile smoking is far greater than that of alcohol drinking compared with most western societies. The widespread use of narghile smoking, particularly

Table III. Frequency of narghile smoking among male and female patients with oral cancer and its relationship with average age at diagnosis

	Regular smoker		*Occasional smoker*		*Nonsmoker*		
	No.	*Mean (SD)*	*No.*	*Mean (SD)*	*No.*	*Mean (SD)*	*P*
Gender							
Male	16	46.0 (11.8)	6	49.8 (11.3)	47	62.1* (16.8)	.001
Female	11	43.8 (10.1)	4	51.3 (17.8)	18	63.5* (18.8)	.000
Total (male and female)	27	45.0 (11)	10	52.0 (13.7)	65	65 (17.3)	

Regular, daily use or a few times per week to a few times per month; *occasional*, a few times in a year.
*Based on independent *t* test.

Table IV. Association between age at diagnosis and independent factors

Variables	*n*	*Age (y) at time of diagnosis, mean (SD)*	*P*
Gender			.46
Male	69	57.3 (15.9)	
Female	33	55.5 (18.4)	
Cigarette smoking			.77
Yes	67	56.3 (15.7)	
No	35	57.5 (19.1)	
Narghile frequency			
Regular	27	45.2 (10.2)*	.03
Occasional	10	50.4 (14.1)	
Nonsmokers	65	62.5 (15.2)	
Both narghile and cigarette smoking			.02
Yes	22	44.9 (9.6)*	
No	20	63.8 (13.5)	
Alcohol			.86
Yes	17	57.3 (10.8)	
No	86	56.6 (16.3)	

*Based on analysis of variance.

Table V. Multiple regression analysis for the association between age at diagnosis and independent factors

Variable	B	*95% CI*	*P*
Gender Female*/Male	−0.88	−7.56 to 5.79	.79
Cigarette smoking No*/Yes	1.79	−6.0 to 9.58	.65
Regular narghile Smoking No*/Yes	−16.44	−26.33 to −6.55	.001†
Occasional narghile Smoking No*/Yes	−11.79	−23.29 to −0.27	.045†
Both cigarettes and narghile No*/Yes	−1.99	−13.84 to 9.86	.74
Alcohol No*/Yes	−1.86	−9.93 to 6.2	.65

R^2 for the model = 0.22.
*Reference category.
†Statistically significant.

among young Jordanians, necessitates studying whether an association exists between this smoking method and the age of oral cancer diagnosis.

This study found that narghile smoking has a significant inverse relationship with age of oral cancer diagnosis, which was independent from other risk factors known to be associated with oral cancer. It also found that 66% of the participants were cigarette smokers, which is a higher figure than those reported in previous studies.[27,35] For example, Khader and Alsadi[35] reported a prevalence of cigarette smoking among Jordanian university students of 35%, and Khabour et al.[27] found the prevalence to be 29%. The higher percentage in our sample can be attributed to selection bias, because our cohort included patients of all ages with oral cancer, whereas previous studies were conducted among healthy young university students.

Alcohol was consumed by 16% of our participants, and although no epidemiologic studies were conducted specifically to assess alcohol consumption in Jordan, a global alcohol use survey found that the per capita consumption of pure alcohol in Jordan was among the least in the world, with an annual estimate of around 0.11 L. The same report estimated the overall percentage of abstainers to be 86% (74% and 98% for men and women, respectively).[36]

Interestingly, 36% of our participants were narghile smokers, a figure close to that reported in healthy young people. For example, Azab et al. found that more than 40% of Jordanian university students were narghile smokers,[28] and Khabour et al. found the prevalence in the same population to be 30%.[27] Additionally, a relatively high percentage of narghile smokers in our sample were women (40%), a figure close to those reported in the literature on healthy populations. For example, Dar Odeh et al. found that female university students prefer narghile smoking as opposed to cigarette smoking (53% vs 33%, respectively).[20]

Despite the relatively small number of studies, an association between narghile smoking and cancer was found. Sajid et al. found that narghile smokers had elevated levels of the tumor marker carcinoembryonic antigen,[37] and several carcinogens (such as phenol, phenol derivatives, polyaromatic hydrocarbons, and carbon monoxide) were found in alarming amounts in the smoke generated by narghile.[38-41] Considering the

similarity of chemical constituents in both narghile and cigarettes, an association between narghile and oral squamous cell carcinoma has been hypothesized,[42] and in particular, early neoplastic changes were seen in oral epithelial cells of narghile smokers.[43]

Our results indicated an inverse relationship between the age at oral cancer diagnosis and the frequency of narghile smoking (Table IV). The more frequently patients with oral cancer smoked narghile, the younger they were when diagnosed with cancer. This relationship was significant for both narghile alone and the combined use of narghile and cigarette smoking. Also, regular and occasional use of narghile were risk factors independent of other risk factors for developing oral cancer at an earlier age (Table V).

The findings of this research are important considering that narghile is commonly perceived as a safe form of smoked tobacco. The results, being based on cohort data analyzed retrospectively, raise the potential concern of recall bias. Although this bias cannot be entirely ruled out, it can be argued that the observed age difference of 16 years between narghile smokers and nonsmokers limits this bias as a factor. Moreover, we attempted to minimize potential inaccuracy in reporting the use of tobacco and alcohol by carefully selecting the interviewers, who are both employees at the National Cancer Registry and are specifically trained in data collection from patients with cancer for the Registry's records.

The relatively small sample size (102 patients) raises another concern over the generalizability of our results. However, the demographic data of this sample are consistent with global data on oral cancer, with a male-to-female ratio of approximately 2:1 and a mean age of approximately 58 years. This makes our conclusion of an independent association between age and frequency of narghile smoking more plausible.

Another limitation to the generalizability of our results is the nonhomogeneous nature of narghile use in terms of the tobacco quantity and concentration, the duration of each smoking session, and the wide variety of additives (such as flavors) that are added to the narghile's tobacco. The fact that narghile is one method of tobacco smoking that is often homemade further limits generalizability. Taking these variables into consideration, a true cause-effect relationship can only be established by prospective studies performed under controlled conditions.

CONCLUSION

The increasing prevalence of narghile smoking among the youth puts them at risk of getting narghile-related diseases at a younger age. Based on the results of this retrospective study of Jordanian survivors of oral cancer, narghile smoking was independently associated with the development of oral cancer at a younger age. Tobacco and oral cancer awareness programs should target young people, and narghile smoking should be subjected to stricter control and further study.

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